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Role of *Helicobacter pylori* Infection in Recurrent Abdominal Pain of the Child in Brazzaville

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Abstract

The *Helicobacter pylori* (Hp) infection is a public health problem, especially in developing countries. However, the responsibility of Hp for the occurrence of recurrent abdominal pain is still unclear. **Objectives**: To determine the prevalence of *Helicobacter pylori* (Hp) infection in children with recurrent abdominal pain (RAP) in Brazzaville and to establish the relationship between Hp infection and RAP. **Patients and Methods:** We conducted a cross-sectional case-control study, between March and September 2018, including 106 children with RAP and 218 children without RAP, aged 2 to 17 years old, received in health centres in Brazzaville. All the children were subjected to detection of Hp fecal antigen by qualitative immuno-chromatography in the faeces. **Results:** The prevalence of Hp infection among children with RAP in Brazzaville was 43.4%. The female sex was most represented in both populations, with a sex ratio of 0.84 in the infected population. Compared with controls, these were children with a mean age of 8.13 ± 4.57 years. Infected children with RAP were unschooled in 66.7% (n = 31) of cases (p < 0.05). Those using potty were 63% (n = 29). Handwashing before meals and after using the toilet was not done in 66.7% (n = 31) and 56.5% (n = 26) of cases, respectively. The proportions were almost similar in the control population. The epigastric site of pain was found in 51.8% of children infected with RAP, the association between Hp infection and the site of pain was statistically significant (p = 0.009). The epidemiological factors influencing Hp infestation in children were identical in both groups, those factors were: age

(OR = 0.61; p < 0.04), education level (OR = 0.35; p < 0.01) of the children and guardian's age (OR = 1.22; p < 0.03), type of toilet (OR = 2.37; p < 0.02) and hand washing (OR = 1; p < 0.01). No statistically significant association was found between Hp infection and RAP (p = 0.10). **Conclusion**: Hp infection is common among children with RAP in Brazzaville. It is favoured by young age and lack of hygiene. The cause and effect relationship between Hp and RAP has not been found. Nevertheless, the search for Hp fecal antigen in children with RAP should be recommended in order to improve the management of this pathology.

Keywords

Helicobacter pylori, Recurrent Abdominal Pain, Fecal Antigen, Child, Brazzaville

1. Introduction

Helicobacter pylori (Hp) infection is caused by a gram-negative, microaerophilic, spiral and helical shape bacterium of the genus Helicobacter with genomic diversity [1]. It is a public health problem, especially in developing countries [2] [2]. Prevalence varies between 1% and 30% in developed countries [4], however in sub-Saharan African countries including Congo, prevalence is over 40% in paediatric populations [5] [6] [7] [8]. Contamination is essentially oral-oral or fecal-oral in childhood. The bacterium colonises the gastric mucosa for a long time and causes acute, even chronic inflammation, which is responsible for various clinical manifestations, some of which have a very serious evolution towards peptic ulcer or gastric cancer [1] [4] [9]. The diagnosis of Hp infection is easy in children and is based preferably on the search for Hp monoclonal antigens (Ag) in the stool [10] [11]. Recurrent abdominal pain (RAP) is frequently observed in children in the range of 40% - 90% [12]. However, the responsibility of Hp for the occurrence of recurrent abdominal pain is still unclear, despite the fact that some authors believe that the presence of CagA+ strain may be responsible for the recurrent abdominal pain in infected children [13]. Assuming that precariousness is an important predictive factor, and that the RAPs are due to a high Hp infestation, it is likely that the presence of the Cytoxin associated gene A (CagA) strain would be the cause of the RAP in infected children [14]. We proposed to carry out this work, the main objective of which is to improve the management of childhood RAP in Brazzaville, more specifically, to determine the prevalence of Hp infection in children with RAP in Brazzaville, to identify the factors influencing the occurrence of infection in these children and to establish the relationship between Hp infection and RAP.

2. Patients and Methods

We conducted a cross-sectional case-control study, between March and Sep-

tember 2018, *i.e.* 7 months in the paediatric wards of Brazzaville hospitals, including the hospital teaching university, the Pierre Mobengo Central Army Hospital, the Base Hospital of Makelekelé, the Talangai Reference Hospital, the Marien Ngouabi Paediatric Hospital, and the Sino-Congolese Friendship Hospital of M'Filou. The study population consisted of all children seen for RAP in the centres selected for the study (case population) and children without RAP (control population) during the study period.

In the case population, we included children aged between 2 and 17 years old, presenting with RAP, that is at least three episodes of abdominal pain during a 3 month period, with an intensity that interferes with the child's everyday life and activity. We did not include children with abdominal pain related to a known pathology for which they were being monitored. In the control population, children with the same age group were included. Children with abdominal pain syndrome and those who had been on proton pump inhibitors, antisecretory agents and antibiotics for at least one month were not included in the study. Informed consent from guardians was mandatory for all children selected. We obtained the consent from the ethics committee for health sciences research in Congo (decision n° 062/MRSIT/IRSSA/CERSSA), prior to the study. The children were systematically enrolled as they were screened following a triple epidemiological, clinical and etiological investigation, which enabled us to obtain, after matching one case of RAP for two controls, a consecutive sample of 318 children divided into two groups. Group 1 (cases: 106 children with RAP) and group 2 (controls: 212 children without RAP). Data were collected on a pre-determined survey sheet. The study variables were sociodemographic (sex, age, education, household size and socio-economic level of the family), lifestyle (type of toilet, water source, hand washing before and after meals and after using the toilet), clinical (location and type of abdominal pain, associated signs such as vomiting, signs of gastroesophageal reflux disease, gastrointestinal haemorrhage) and biological (detection of Hp monoclonal Ag in fresh stools). We defined the latrine as a pit dug in loose soil, without a drainage system, covered either by an assembly of branches or by a concrete slab centred by a hole for the passage of excreta. The modern toilet is a sanitary facility with a flushing or siphon system to evacuate excreta into a septic tank. The chamber pot, commonly known as a potty, is a container with or without a lid on which the child sits to relieve himself or herself and then the contents are emptied into the toilet. We have considered tap water as a source of water, which is generally potable because it is regulated by the national water company. It becomes private tap water when it is distributed directly to a household or public tap water when it is available to a large number of households; well water, which is non-potable water, rises to ground level by means of a bucket or manual pump; spring water meets the same requirements as natural water, with the difference that its mineral salt and trace element content is not stable. Fresh faeces was defined as freshly emitted faecal matter, collected in a fixed booth at the survey site, without any preparation, and sent to the laboratory up to one hour after the end of the collection, away from excessive

heat. Sometimes the faeces were kept in a cool place between 2˚C and 8˚C for 48 hours before analysis. The search for Hp monoclonal Ag was carried out in fresh faeces using strips of the *CerTestR H. Pylori rapid diagnostic test* (RDT) based on the principle of immuno-chromatography. The judgement criteria were the detection of fecal Hp Ag by the presence of one (negative result) or two (positive result) lines on the RDT strip.

Data were captured and processed using CS pro Version 7.1, SPSS 21 and Microsoft Excel 2016. Qualitative variables were presented in numbers and percentages in parentheses. Quantitative variables were expressed as mean ± standard deviation. The comparison of qualitative variables used Pearson's chi-square test, while the comparison of quantitative variables used Student's t-test. A bivariate analysis established the correlation between the dependent variable (health phenomenon studied) and the presence of certain factors (independent variable) with calculation of odds ratio (OR) and with 95% confidence intervals derived using the test-based method. (In most situations, the odds ratio provides a good approximation of the relative risk, *i.e.*, the risk of recurrent abdominal pain in children with H pylori infection, compared with the risk in uninfected children). For the comparisons, the significance threshold was <0.05.

3. Results

Out of a total of 318 cases, 106 children included had RAP, of which 64 cases (60.4%) were girls and 42 cases (39.6%) boys; in 46 of these cases, the Hp fecal Ag test was positive, thus a prevalence of 43.4% (46/106). In contrast, the prevalence of Hp in children without RAP was 35.8% (76/212). Females were most represented in both populations, with a sex ratio of 0.84 in the infected population with RAP and 0.49 in the population of infected children without RAP (139/212). The mean age of infected children with RAP was 8.13 ± 4.57 years (extremes: 2 and 17 years) and those under 5 years of age accounted for 57.1% (p < 0.05). Infected children with RAP were unschooled in 66.7% (n = 31) of cases (p < 0.05) and lived in a 1 - 4 persons household in 53.8% of cases; the average household size was 6.33 ± 2.38 persons (extremes: 2 and 11) (p < 0.05). Compared to controls, the average age of children was 8.34 ± 4.63 years, 48.9% were unschooled (p = 0.05) and 47.1% lived in a household of 2 - 4 people (extremes of 2 and 13). The average age of guardians of infected children with RAP was 42.09 ± 8.89 years (extremes: 24 and 64 years). Children with guardians aged 35 - 44 years accounted for 52.4% (n = 22; P = 0.03); while in the control population it was 40.53 ± 11.08 (extremes: 17 and 66 years) and for 29 (46.8%) of the children the parents were younger than 35 years of age (P < 0.04). In the case population, the children belonged to a family of average socio-economic level (n = 71), *i.e.* 66.7%, low (45), *i.e.* 42%, and high (n = 21), *i.e.* 20%. They were of low socio-economic level (n = 88) (41.3%), medium (n = 72) (33.9%) and high (n = 27) (12.5%) among the controls. The distribution of children according to lifestyle habits in the two populations is recorded in Table 1 and Table 2 (variables are expressed in numbers and percentages in brackets). After logistic regression,

the factors influencing the acquisition of Hp infection in children with RAP are shown in Table 3. Clinically, constant abdominal pain in all infected children was epigastric (51.8%), periumbilical (40.7%) or diffuse (40%), rarely hypochondrial. A type of burn (58.6%), cramping (48.3%), unspecified (36.4%) and compressive (26.9%). Among the associated signs, nausea and vomiting were observed in 39 (54.1%) children with p < 0.03, hematemesis in 3 children (60%), melena in 2 children (66.7%), early satiety in 5 children (55.6%), gastric fullness in 4 children (57.1%), eructation in 3 cases (42.9%) and pyrosis in 1 (50%) case. Table 4 shows the results of the bivariate analysis between the case and control populations.

Table 1. Lifestyle patterns of children with RAP with fecal HpAg positive (cases).

Facteurs	Positive (n; %)	Negative (n; %)	OR (95%)	P
Type of toilets				
- Modern toilet	12 (25)	45 (75)	0.30 (0.14 - 0.64)	<0.001
- Pit toilet	20 (44.2)	33 (55.8)	1 (0.51 - 1.97)	<0.98
- Chamber pot	29 (62.5)	23 (37.5)	3.07 (1.54 - 6.09)	<0.001
Water source				
- Public tap	22 (47.5)	32 (52.5)	1.31 (0.69 - 2.47)	<0.40
- Private tap	17 (37.5)	38 (62.5)	0.80 (0.41 - 1.54)	<0.51
- Spring water	20 (42.9)	34 (57.1)	1.09 (0.57 - 2.07)	<0.78
- Well	18 (40)	36 (60)	0.88 (0.46 - 1.68)	<0.70
Hand washing				
- Before meal	18 (38.6)	37 (61.4)	0.31 (0.14 - 0.69)	<0.004
- After meal	18 (39.8)	36 (60.2)	0.28 (0.12 - 0.63)	<0.002
- After toilet	15 (33.3)	40 (66.7)	0.37 (0.16 - 0.83)	<0.016

Table 2. Lifestyle patterns of children without RAP with fecal HpAg positive (controls).

Factors	Positive (n; %)	Negative (n; %)	OR (IC: 95%)	P
Type of toilet				
- Modern toilet	19 (25.4)	101 (74.6)	0.37 (0.21 - 0.65)	<0.0007
- Latrine	29 (38.1)	84 (61.9)	0.89 (0.53 - 1.48)	<0.65
- Chamber pot	43 (56.5)	59 (43.5)	2 (1.69 - 4.65)	<0.0001
Water source				
- Public tap	32 (41.6)	79 (58.4)	2.07 (1.26 - 3.40)	<0.004
- Private tap	24 (31.7)	93 (68.3)	1.10 (0.65 - 1.86)	<0.69
- Spring	17 (22.2)	105 (77.8)	0.60 (0.34 - 1.07)	<0.08
- Well	18 (23.5)	104 (76.5)	0.65 (0.37 - 1.15)	<0.14
Hand washing				
- Before meal	24 (31.4)	93 (68.6)	0.48 (0.26 - 0.88)	<0.01
- After meal	21 (28)	98 (72)	0.31 (0.17 - 0.56)	<0.0001
- After toilet	22 (28.9)	97 (71.1)	0.42 (0.23 - 0.79)	<0.006

Table 3. Epidemiological factors influencing acquisition of Hp infection.

Explanatory variables	Fecal Hp Ag test result				
	Positive (n = 46; %)	Negative (n = 60; %)	OR (IC-95%)	Chi square	p
Age: 5 - 9 years	18 (45)	22 (55)	0.61 [0.22 - 1.78]	2.8	0.04
Primary education level	22 (41.2)	21 (58.5)	0.35 [0.12 - 1.09]	6.4	0.01
Guardian age: 35 - 44 years	22 (52.4)	20 (47.6)	1.22 [0.42 - 3.62]	3.5	0.03
Type of toilet (chamber pot)	38 (44.2)	48 (55.8)	2.37 [0.61 - 9.38]	2.8	0.02
Hand washing					
- Before meal	12 (66.7)	6 (33.3)	1	4.7	1
- After meal	9 (69.2)	4 (30.8)	1	4.02	0.04
- After toilet	26 (56.5)	20 (43.5)	1	5.7	0.01

Table 4. Impact of *Hp* infection in RAP.

Population	number	Fecal Hp Ag test result		p
		Positive (n; %)	Negative (n; %)	
Case	106	46 (43.4)	60 (56.6)	0.10
control	212	76 (35.5)	136 (64.2)	

4. Discussion

We report the results of a comparative cross-sectional study on the role of Hp infection in the occurrence of RAP in infected children in Brazzaville; on two series of children, the first with RAP and the second without RAP. Based on the hypothesis that in Congo, precariousness would be a predictive factor and that RAP would be due to high Hp infestation. The inclusion criteria were sufficiently clear to avoid bias in the interpretation of the results. However, this study has limitations; on the one hand, this survey limited only to urban areas should be considered as preliminary work. As the survey was cross-sectional, it was not possible to estimate the temporal sequence between Hp and RAP, and therefore it did not allow a direct estimation of the risk. On the other hand, we admit a selection bias because participation in the study was on a voluntary basis and the RAPs were not a frequent reason for consultation during our study period.

The prevalence of Hp infection in children with RAP is 43.4%. Our result is similar to those of Franck and coll. in Switzerland [14] and Masoodpoor and coll. in Iran [15] who reported 40% each. However, it is lower than that of Sebanjo and coll. in Nigeria, 63.6% [16]. However, Kumar and Mohsen and coll. reported lower prevalences [17] [18]. This discrepancy could be explained by methodological differences in sampling, ethnic and environmental factors, and the method of detection of Hp Ag. Comparison between the two types of populations revealed similarities in age, gender, education and age of guardian. Indeed, children between the ages of 5 and 9 years were the most infected with a

mean age of 8.13 ± 4.57 years. The relationship between age and Hp infection was statistically significant (p < 0.05). Our result is superimposable to that of Alimohammadi and coll. in Iran [19] and Punhal *et al.* in Pakistan [20]. However Ozen *et al.* in Turkey [21] and Masoodpoor [15] report a higher mean age probably due to the difference in the selected age groups and the sample size. The majority of infected children were not attending school, with a predominance of cases (66.7%) compared to 53.8% of controls. Our results could be explained by the fact that the unschooled children were in the under-5 age group. We found a significant relationship between Hp and education level. Children with young guardians were the most infected in our study. Our results could be explained by the inexperience and/or unavailability of young parents in the education of the children. However, Ategbo *et al.* in Gabon did not find a statistical correlation between Hp and age of the guardian [6]. Children using latrines and especially chamber pots were the most infected in both study populations with a statistically significant association (OR = 2.37; p < 0.02). Etukudo *et al.* in Nigeria made the same observation [22]. This result, which can be superimposable on our own, can be explained by the precariousness of households in some African countries. Similarly, both in the case and control populations, children using public tap water were more infected with Hp. However, no significant difference was observed between Hp and the water source (p > 0.005). Nevertheless, the association between Hp infection and hand washing before, after meals and after toilet use was statistically significant (Table 3). These results could be explained by the poor hygiene and living conditions of the Congolese population as reported by the Congo Demographic and Health Survey report [23]. Epigastric pain was prevalent among infected children with ARD. The association between Hp infection and the site of pain was statically significant (p < 0.005). Our finding is superimposable to that of Senbanjo. This is due to the gastric tropism of the bacterium. Moreover, the existence of epigastralgia would be the only symptom of pseudo-ulcer dyspepsia, which is poorly appreciated in young children who express themselves poorly. Vomiting was the only symptom with a statistically significant association with Hp infection (p < 0.05). Vomiting would be a predictor of gastrooral contamination in our country.

Logistic regression found that the epidemiological factors favouring the acquisition of Hp infection in children were identical in the two types of populations; namely, age between 5 and 9 years of age, level of education of the children, age of the guardian between 35 and 44 years of age, type of toilet and lack of handwashing. The major predictive factor with higher risk in children was the use of chamber pots (OR = 2.37; p = 0.02). We observe a similarity of results with those of Senbanjo and Shaker *et al.* in India regarding age [16] [24]. The diversity observed for the other factors could be justified by the choice of variables in each of these studies.

The authors' opinions are still controversial on the existence of a close relationship between RAPs and Hp [14] [25]. The bivariate analysis between cases and controls did not reveal a statistical association between Hp infection and

RAPs with respect to the required significance level, although the association was real in 10% of cases (p > 0.05). Our results are consistent with those of many studies [15] [26] [27]. However, other authors have found a correlation between Hp and RAP [18] [19] [21] [24]. This difference could be justified by the type of cross-sectional study that did not allow to estimate the temporal sequence between Hp and RAP *i.e.* whether the factors studied preceded the infection or vice versa, the small sample size, the method of detection of Hp infection and the surrounding factors. Our results suggest that the presence of Hp infection in RAPs should be an argument for the "test and treat" strategy because of the high frequency of this infection in developing countries.

5. Conclusion

Hp infection is common among children with RAP in Brazzaville. It is favoured by young age and lack of hygiene. The cause-effect relationship between Hp and RAP has not been found, although it is real in 10% of cases. Nevertheless, the search for Hp faecal antigen in children with RAP should be recommended in order to improve the management of this pathology and to prevent complications related to Hp infection in young persons.

Conflicts of Interest

The authors declare no conflicts of interest with respect to the publication of this article.

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Survey Sheet

Role of *helicobacter pylori* infection in recurring abdominal pain in children in Brazzaville

Date of investigation: |__|__|__|__|__|__| **N° of sheet:** |__|__|__|

Hospitalized patient: [____]

Patient seen in consultation: [____]

1) Epidémiological parameters

- Sex:

  M [_____]

  W [_____]

- Date of birth: |__|__|__|__|__|__| et/ou Age: …………………………ans

- School level:

  Préschool [_____]

  Primary [_____]

  Secondary [_____]

  Unschooled [_____]

  Others [_____]

- Dwelling place: ……………………………

- Child custody:

  Mother father [_____]

  Grand-mother [_____]

- Age of primary guardian…………………………

- Number of people living under the same roof: |__|__|

2) Habits (multiple answers possible)

- Type of latrine:

  Modern [_____]

  Traditionnal [_____]

  Public [_____]

  Private [_____]

  Both [_____]

- Water source:

  Public tap [_____]

  Spring water [_____]

  Modern wells [_____]

  Private faucet [_____]

- Other sources to be specified: …………………………

- Hand washing:

  Meal: Before [_____] After [_____]

  Toilet: Before [_____] After [_____]

3) Clinical parameters (Several answers possible)

a) Antecedent

i) personnal

- Gastric ulcer:

Yes ☐

No ☐

Without precision ☐

- Duodenal ulcer:

Yes ☐

No ☐

Without precision ☐

- Gastric cancer:

Yes ☐

No ☐

Without precision ☐

- Others to be specifised: …………………………

ii) Family

- Gastricand/or duodenal:

Yes ☐

No ☐

- Gastric:

Yes ☐

No ☐

b) Digestive symptoms

- Pain type:

Burning ☐

Cramping ☐

Compression ☐

- Site of pain:

Epigastrium ☐

Right hypochondrium ☐

Diffuse ☐

Left hypochondrium ☐

Others to specify…………………………

- Nausea

Yes ☐

No ☐

- Early feeling of fullness

Yes ☐

No ☐

- Sensation of gastric fullness

Yes ☐

No ☐

- Belching

Yes ☐

No ☐

- Pyrosis

Yes ☐

No ☐

- Regurgitation

Yes ☐

No ☐

- Vomiting

Yes ☐

No ☐

- Haematemesis

Yes ☐

No ☐

- Melena

Yes ☐

No ☐

- Other digestive symptoms to be specified…………………………

4) Biological parameters

- Results of the test for the detection of Ag H. pylori in the stool:

Positive ☐

Negative ☐